09/857906
JC03 Rec'd PCT/PTC 09 JUN 2001

RESPONSE TO WRITTEN OPINION IN PCT/US99/29091

AUTHORIZED OFFICER A.T. NGUYEN
IPEA/US
COMMISSIONER OF PATENTS AND TRADEMARKS — VIA FAX
BOX PCT — MAIL CONFIRMATION
WASHINGTON, D.C. 20231

RE.: **PCT/US99/29091 – RESPONSE TO WRITTEN OPINION**

Dear Authorized Officer Nguyen:

This is in response to the Written Opinion in the captioned PCT application, mailed on 14 February 2001. As this response is being transmitted to your attention on April 16, 2001, since April 14, 2001 was a Saturday, this response is being timely filed. Please take into account the comments and amendments provided herein in the formulation of the International Preliminary Examination Report in this case. We believe the remarks and amendments provided herein address the opinion stated with respect to novelty and inventive step in the 14 February 2001 Written Opinion.

1. Novelty:

The novelty of all claims in this application, except for claim 8, has been acknowledged. It is stated that claim 8 lacks novelty as being anticipated by Blank, et al., US Patent 5,035,892. Provided herewith is a replacement page 8 of the subject application, wherein claim 8 is amended to recite the limitation that the "plurality of antimicrobials compounds to the enhanced surface area of said polymer matrix" is attached "by non-siloxane bonds". Accordingly, it is urged that the requirements of novelty are met for claim 8 as amended, in much the same manner as novelty of claims 1-7 has been met.

2. Inventive Step:

The inventive step of claims 1-8 in this application is challenged as these claims are said to be obvious in light of Blank et al, US Patent 5,035,892. It is stated that Blank et al., disclose the invention substantially as claimed except for specifying the compounds being coupled by non-siloxane bonds to the polymer matrix. The Written Opinion acknowledges that Blank et al. disclose that the bonding with silane "is to provide the benefits of odor reduction." Without stating more, the Written Opinion goes on to state that "it would have been obvious to one skilled in this art the [to?] bond the matrix with non-siloxane bonds when the superabsorbent in [is?] to be exposed to acids."

In response, it is urged that it is incumbent on the Authorized Office in establishing the International Preliminary Examination Report (IPER), to state a firm basis on which it is believed to be obvious to bond the antimicrobials to the matrix via non-siloxane bonds, when the teaching in the cited reference makes specific reference only to siloxane bonds, and makes no mention of non-siloxane bonds, or the need to avoid exposure to acid or alkali or the like.

Further, it is urged that in considering the question of inventive step with respect to claims 1-8 in this application, that the following considerations are pertinent. Consideration of these comments in the establishment of the IPER is respectfully requested:

US patent # 5,045,322; Blank et al. pertains to attachment of monomeric siloxane-based quaternary compounds to SAPs. The siloxane-based compounds are also sensitive to hydrolysis, as noted in the present application. The siloxane compound Blank describes is expected to be more easily hydrolyzed than the acrylate polymers used in the present application. Furthermore, other polymers used in the present invention (such as those based on DADMAC or trialkyl(p-vinylbenzyl) ammonium chloride) are totally stable towards hydrolysis.

The antimicrobial effectiveness of a large molecule like the siloxane used by Blank is reduced somewhat by its steric hindrance. Since it can and does fold on itself, the number of such molecules that can be bonded to a given surface is limited as compared to smaller molecules. Further, the fact that the nitrogen atom can be blocked by other atoms in the molecule limits its positive charge density as well. The consequence of this is that the antimicrobial is less effective than one that can be attached to the same surface in greater numbers or density per unit area. Since the net positive charge on the nitrogen atom is related to the effectiveness of the antimicrobial, one that has more exposed positive atoms would theoretically be more effective. This can be shown by comparing the effectiveness of the Blank compounds to any other quaternary that has less steric hindrance. The result is that in the presence of proteinaceous matter such as blood, urine and tissue cells the Blank compound can be blinded more easily than any other quaternary that has a greater number of unhindered net positive charges. See PCT/US99/29091 line 20 of the Summary of the Invention.

A further shortcoming of the siloxane quaternary materials disclosed according to Blank et al., is that it only provides an active monolayer coverage of the surface. That is, the molecules are not long-chain polymers. By contrast, the surface according to the present invention is covered with polymeric chains of quaternary materials. Polymeric antimicrobials used according to the present invention are more effective than the monomeric antimicrobials described by Blank, (see Chen, Z. C., et al., "*Quaternary Ammonium Functionalized Poly(propylene imine) Dendrimers as Effective Antimicrobials: Structure-Activity Studies*", Biomacromolecules 1, p473-480 (2000); Ikeda, T., "*Antibacterial Activity of Polycationic Biocides*", Chapter 42, page 743 in: High Performance Biomaterials, M. Szycher, ed., Technomic, Lancaster PA, (1991); Donaruma, L. G., et al., "*Anionic Polymeric Drugs*", John Wiley & Son, New York, (1978)). Thus, in order to obtain a high antimicrobial activity, a high surface area base material must be used with the siloxane quaternary materials. The Blank patent describes placing this monolayer antimicrobial treatment onto powders, which are then used to make superabsorbent polymer gels. The powder has a very high surface area, and hence the gels contain a lot of antimicrobial. However, the Blank gels have almost zero mechanical strength, (and must be contained inside some type of matrix in order to form

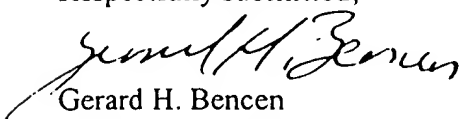
a useable device). In contrast, the modified cellulose fibers of the present invention have inherent mechanical properties which allow them to be directly used as structural devices such as bandages.

The present application further discloses "enhanced surface area", see page 6, lines 3 to 16. The description of "enhanced surface area" would not apply to monolayer treatments such as the siloxane system described by Blank. That is, an enhanced surface area substrate is needed to achieve high quaternary content. According to the present invention, however, a high quaternary content may be achieved even on low surface area fibers such as cotton because the quaternary materials of the present invention are polymeric. The present applicants have actually attempted use of a Dow Corning product (TMS - the same compound described by Blank) to treat fabrics, and have found that a significantly lower amount of quaternary antimicrobial groups could be applied. The bactericidal activity of the TMC treated fabrics was several orders of magnitude lower than the fabrics treated with polymeric quaternary materials. The applicant further found that the TMC-treated samples became water-repellent. This effect was reported by Blank (see US Patent 5,035,892; column 12, line 57). This impairment of absorbency is undesirable in a product intended for use as an absorbent. Furthermore, the siloxane monomer has a higher MW than the monomers of the present invention. As a result, the effective quaternary material content (number of positively-charged sites per gram of material) is further reduced as compared to that of the present invention. Finally, the present application further discloses use of neutral or negatively charged antimicrobial polymers, which is neither disclosed nor suggested according to Blank, et al.

In light of all of the foregoing distinctions, it is respectfully urged that the present invention provides non-obvious advantages over that which is disclosed according to Blank, et al. Accordingly, it is respectfully requested that the foregoing distinctions, comments, and advantages of the present invention be taken into account in establishment of an IPER reflecting both the novelty and inventive step compliance of all claims in this application.

Should the Authorized Office have any comments, questions or concerns in connection with the remarks and amendment provided herein, it is respectfully requested that the undersigned should be contacted such that the requested positive IPER may be established.

Respectfully submitted,



Gerard H. Bencen
Attorney for Applicant
Bencen & Van Dyke, P.A.
1630 Hillcrest Street
Orlando, Florida 32803
Phone: 407-228-0328
Fax: 407-228-0329

We claim:

1. A dressing for absorbing biological fluids, comprising:

a superabsorbent polymer matrix having an enhanced surface area; and

a plurality of antimicrobial compounds coupled by non-siloxane bonds to said polymer matrix.

2. A dressing as recited in claim 1, wherein said plurality of antimicrobial compounds comprise quaternary ammonium compounds.

3. A dressing as recited in claim 1, wherein said antimicrobial compounds comprise chain-like structures tethered at one end to said polymer matrix.

4. A dressing as recited in claim 1, wherein said plurality of antimicrobial compounds are non-ionic compounds.

5. A dressing as recited in claim 1, wherein said dressing comprises a sanitary pad.

6. A dressing as recited in claim 1, wherein said dressing comprises a tampon.

7. A dressing as recited in claim 1, wherein said dressing comprises a bandage.

8. A method for fabricating an intrinsically antimicrobial absorbent dressing, comprising the steps of:

forming a superabsorbent synthetic polymer matrix having an enhanced surface area; and

attaching by non-siloxane bonds a plurality of antimicrobial compounds to the enhanced surface area of said polymer matrix.

We claim:

1. A dressing for absorbing biological fluids, comprising:

a superabsorbent polymer matrix having an enhanced surface area; and

a plurality of antimicrobial compounds coupled by non-siloxane bonds to said polymer matrix.

2. A dressing as recited in claim 1, wherein said plurality of antimicrobial compounds comprise quaternary ammonium compounds.

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7. A dressing as recited in claim 1, wherein said dressing comprises a bandage.

8. A method for fabricating an intrinsically antimicrobial absorbent dressing, comprising the steps of:

forming a superabsorbent synthetic polymer matrix having an enhanced surface area; and

attaching a plurality of antimicrobial compounds to the enhanced surface area of said polymer matrix.

Bencen & Van Dyke, P.A.

Intellectual Property Law

1630 Hillcrest Street, Orlando, Florida 32803, USA
Phone: (407) 228-0328;Fax: (407) 228-0329; bvdlaw@yahoo.com

FACSIMILE COVER SHEET

TO	:	Authorized Officer Hallet Saunders
COMPANY	:	IPEA/US UNDER THE PCT AT THE USPTO
FAX No.	:	703-305-3230
No of PAGES	:	3 (including coversheet)
FROM	:	Timothy H. Van Dyke
DATE	:	June 5, 2001
RE	:	PCT/US99/29091 – REVISED RESPONSE TO WRITTEN OPINION Our Docket No: QMT-1 PCT

VIA FACSIMILE ONLY

AUTHORIZED OFFICER SAUNDERS:

In response to the PCT Communication dated May 24, 2001(copy attached), enclosed herewith is a revised page 8 of the response to the written opinion for the above-referenced application. I spoke to Examiner Nguyen on June 4, 2001, and he informed me that the only issue with the response was that the replacement sheet for the amended claims was illegible. He instructed me to send you a clean replacement sheet. I trust that this letter satisfies any outstanding problems with our earlier filed response and that it will be appropriately processed. Please contact me immediately if you have any other questions or concerns.

Sincerely,

Timothy H. Van Dyke

TVD/mkk
Attachments

If you do not receive all pages or if any portion of this transmission is not legible, call the sender at (407) 228-0328.

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

To:
EDWARD J. HANDLER III
KENYON & KENYON
ONE BROADWAY
NEW YORK, NY 10004

COMMUNICATION IN CASES FOR WHICH NO OTHER FORM IS APPLICABLE

Applicant's or agent's file reference: 10088/3	Date of mailing (day/month/year): 24 MAY 2001
International application No.: PCT/US99/29091	REPLY DUE: See paragraph 1 below
Applicant: QUICK-MED TECHNOLOGIES, INC.	International filing date (day/month/year): 08 DEC 99

1. [ ] REPLY DUE within _____ months/days from the above date of mailing
   [ ] NO REPLY DUE
   [X] IMPORTANT COMUNICATION
   [ ] IMPORTANT ONLY

2. COMMUNICATION:
   APPLICANT'S RESPONSE TO THE WRITTEN OPINION WILL NOT BE CONSIDERED IN THAT THE REPLACEMENT SHEET IS NOT LEGIBLE.

Name and mailing address of the IPEA/ Assistant Commissioner for Patent Box PCT Washington, D.C. 20231 Attn:RO/US Facsimile No. 703-305-3230	Authorized officer Hallet A. Saunders Telephone No. 703-305-3663

Form PCT/IPEA/424 (January 1994)

We claim:

1. A dressing for absorbing biological fluids, comprising:
A superabsorbent polymer matrix having an enhanced surface area; and
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2. A dressing as recited in claim 1, wherein said plurality of antimicrobial compounds comprise quaternary ammonium compounds.

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Attaching by non-siloxane bonds a plurality of antimicrobial compounds to the enhanced surface area of said polymer matrix.

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Bencen & Van Dyke, P.A.

Intellectual Property Law

1630 Hillcrest Street, Orlando, Florida 32803, USA
Phone: (407) 228-0328; Fax: (407) 228-0329; bvdlaw@yahoo.com

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Sincerely,

Timothy H. Van Dyke

TVD/mkk
Attachments

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09/857,579

PATENT COOPERATION TREATY

PCT

REC'D 20 JUL 2001
WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 10068/3	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US99/29091	International filing date *(day/month/year)* 08 DECEMBER 1999	Priority date *(day/month/year)* 09 DECEMBER 1998
International Patent Classification (IPC) or national classification and IPC IPC(7): A61F 13/15 and US Cl.: 604/358, 372; 424/443		
Applicant QUICK-MED TECHNOLOGIES, INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 3 sheets.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

   I ☒ Basis of the report

   II ☐ Priority

   III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability

   IV ☐ Lack of unity of invention

   V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   VI ☐ Certain documents cited

   VII ☐ Certain defects in the international application

   VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
20 JUNE 2000	01 JUNE 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer A. T. NGUYEN
Facsimile No. (703) 305-3230	Telephone No. (703) 308-2154

Form PCT/IPEA/409 (cover sheet) (July 1998)*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US99/29091

I. Basis of the report

1. With regard to the elements of the international application:*

[X] the international application as originally filed

[X] the description:
pages 1-6 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the claims:
pages 7 , as originally filed
pages NONE , as amended (together with any statement) under Article 19
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the drawings:
pages NONE , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the sequence listing part of the description:
pages NONE , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in printed form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. [X] The amendments have resulted in the cancellation of:

[X] the description, pages NONE

[X] the claims, Nos. NONE

[X] the drawings, sheets~~/fig~~ NONE

5. [ ] This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

***Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US99/29091

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims	1-8	YES
	Claims	NONE	NO
Inventive Step (IS)	Claims	NONE	YES
	Claims	1-8	NO
Industrial Applicability (IA)	Claims	1-8	YES
	Claims	NONE	NO

2. citations and explanations (Rule 70.7)

Claims 1-8 lack an inventive step under PCT Article 33(3) as being obvious over Blank et al (5,035,892).

Blank et al disclose the invention substantially as claimed (see abstract, col. 7, lines 46-55, and claim 6) except for specifying the compounds being coupled by non-siloxane bonds to the polymer matrix. Blank et al however disclose that the bonding with silane is to provide the benefits of odor reduction. Furthermore, it is of the examiner's position that substituting compounds coupled by siloxane bonds for those without the siloxane bonds is an obvious design choice. Thus, it would have been obvious to one skilled in this art to attach to the superabsorbent polymer matrix with non-siloxane bonds when the superabsorbent in to be exposed to acid, or alkali or the like.

---------- NEW CITATIONS ----------

NONE

PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : A61F 13/15 — A1

(11) International Publication Number: **WO 00/33778**

(43) International Publication Date: 15 June 2000 (15.06.00)

(21) International Application Number: PCT/US99/29091

(22) International Filing Date: 8 December 1999 (08.12.99)

(30) Priority Data:
60/111,472 8 December 1998 (08.12.98) US

(71) Applicants *(for all designated States except US)*: QUICK-MED TECHNOLOGIES, INC. [US/US]; 7844D Lexington Club Boulevard, Del Ray Beach, FL 33446 (US). UNIVERSITY OF FLORIDA RESEARCH FOUNDATION, INC. [US/US]; 223 Grinter Hall, P.O. Box 115500, Gainesville, FL 32611-5500 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: BATICH, Christopher, D. [-/US]; 3733 N.W. 40th Street, Gainesville, FL 32606 (US). SCHULTZ, Gregory, S. [-/US]; 832 N.W. 45th Terrace, Gainesville, FL 32605 (US). MAST, Bruce, A. [-/US]; 5507 N.W. 45th Lane, Gainesville, FL 32606 (US). OLDERMAN, Gerald, M. [-/US]; 17 Pickman Drive, Bedford, MA 07130 (US). LERNER, David [-/US]; 7844D Lexington Club Boulevard, Del Ray Beach, FL 33446 (US).

(74) Agents: HANDLER, Edward, J., III et al.; Kenyon & Kenyon, One Broadway, New York, NY 10004 (US).

(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published

With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: INTRINSICALLY BACTERICIDAL ABSORBENT DRESSING AND METHOD OF FABRICATION

(57) Abstract

A superabsorbent polymer dressing having antimicrobial properties for use in fabricating wound dressings, sanitary napkins, tampons and the like, includes a synthetic polymer matrix fabricated to have an enhanced surface area. Antimicrobial compounds are coupled to the surface of the polymer matrix by non-siloxane bonds.

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Intrinsically Bactericidal Absorbent Dressing and Method of Fabrication

Field of the Invention

This invention relates generally to absorbent dressings, and more particularly highly-absorbent synthetic polymer dressings having antimicrobial agents attached thereto.

Background of the Invention

Bacterial growth in absorbent dressings for wounds, urinary incontinence diapers, and menstruation pads can lead to serious medical complications as well as social difficulties. For example, bacterial growth in urinary incontinence diapers or menstruation pads usually produces strong, unpleasant odors that are socially unacceptable and can cause persons to alter their lifestyle. Conventional absorbent pads for urinary incontinence and menstruation are not inherently bactericidal. Consequently, the only way to avoid growth of bacteria in the absorbent dressings is to change them at frequent intervals, even if the absorbent capacity of the pad has not been reached. In the area of wound dressings, bacterial contamination of acute wounds and infection of chronic skin wounds are major clinical problems that can result in significant morbidity and, in severe cases, mortality. Conventionally, wound dressings have been designed to absorb wound fluids and yet provide a moist environment for promoting wound healing. However, such moist environments create a nutrient rich reservoir for bacterial growth in the dressing. Bacteria growing in the dressing can be shed back into the wound, increasing the risk of wound infection, or response to toxins, and producing strong, foul odors.

In an effort to address these problems, antibiotics or chemical disinfectants are frequently applied topically to wounds prior to covering the wound with a dressing.

Alternatively, topical agents are sometimes applied directly to the surface of the dressing. To control foul odors, some known dressings incorporate charcoal powder to absorb molecules generating the foul odor. For some applications, topical application of antibacterial agents is not desirable. For instance, bactericidal agents applied topically to wound dressings have a tendency to seep into the wound being treated. Furthermore, many antimicrobial drugs, such as iodine, are cytotoxic and will retard wound healing if used repetitively or at high concentrations.

A composition comprising a superabsorbent polymer having a monolayer (or near monolayer) of silane antimicrobial agent in a covalent bonding relationship with the base polymer is disclosed in U.S. Patent No. 5,045,322. The composition may be in the form of flakes, strips, powders, filaments, fibers or films, and may be applied to a substrate in the form of a coating. The aforementioned composition is less apt to enter a wound vis-a-vis conventional topical treatment systems. In that respect, the disclosed composition provides an improvement over conventional topical treatment systems. However, silanes contain siloxane bonds which can be cleaved by acids and bases produced by infection or bacterial growth. In turn, these reactions may weaken or destroy bonds between the silane antimicrobial agent and the underlying polymer. Consequently, antimicrobial agent may seep into a wound and retard wound healing.

The need exists for an improved antimicrobial dressing composition having an antimicrobial agent which can be maintained securely attached to a superabsorbent polymer upon exposure to acids and bases produced by infection and bacterial growth. In addition to reducing the propensity for detachment of the antimicrobial agent, it would be desirable to provide a surface area enhanced dressing structure for increasing the effectiveness of the antimicrobial agent.

Summary of the Invention

It is an object of the present invention to provide an inherently bactericidal superabsorbant dressing having an enhanced surface area.

It is another object of the present invention to provide an inherently bactericidal superabsorbant dressing having an improved bactericidal attachment structure that resists degradation upon exposure to acids or bases produced, for instance, during bacterial growth.

These and other objects are achieved by the inherently bactericidal polymer composition of the present invention. In the preferred embodiment, the composition comprises a polymer matrix having quaternary ammonium groups tethered to its surface through non-siloxane bonds. The surface area of the polymer matrix is enhanced, for instance, by electrostatically spinning a fiber-forming synthetic polymer to form a frayed fiber or filament. Alternatively, the polymer solution can be wet- or dry-spun to create a roughened fiber surface by controlling the choice of solvent and the polymer solution temperature. Additional surface area enhancement is provided by tethering molecular chains of quaternary ammonium pendent groups to the surface of the polymer matrix. Tethering may be accomplished by known techniques such as grafting and selective adsorption.

In an alternate embodiment of the invention, non-ionic bactericidal molecules are coupled to the surface of the polymer matrix, in lieu of ionically-charged molecules. Ionically-charged molecules are prone to being neutralized upon encountering oppositely-charged molecules. For instance, positively-charged quaternary ammonium groups may be neutralized by negatively-charged chloride ions present in physiological fluids. In instances were such neutralization is significant enough to reduce the bactericidal properties of the dressing below an acceptable level, non-ionic surface groups may be preferable.

Detailed Description of the Preferred Embodiments

A novel antibacterial polymer composition is fabricated to have an enhanced surface area and superabsorbent capacity for biological fluids, including urine, blood, and wound exudate.

In the preferred embodiment of the present invention, the composition includes a polymer matrix having quaternary ammonium compounds attached to the surface of the polymer matrix. The polymer matrix is comprised of a plurality of hydrophilic fibers or filaments which can be fabricated in any suitable manner. For example, suitable fibers or filaments can be fabricated by wet- or dry-spinning a fiber-forming synthetic polymer from a spinning solvent. The resulting polymer has superabsorbent capacity. Generally, polymers capable of absorbing from about thirty to sixty grams of water per gram of polymer are considered to be superabsorbent. Examples of superabsorbent polymers which can be fabricated in this manner include polyacrylic acids, polyethylene oxides and polyvinyl alcohols. For example, methods for spinning polyethylene oxide using acetone solvent are well known.

Significantly, the polymer matrix is fabricated to have an enhanced surface area. Enhancing the surface area of the polymer matrix results in improved absorption of biological fluids, and increases the availability of sites for attachment of the antimicrobial quaternary ammonium compounds. A corresponding increase in the quantity and density of antimicrobial sites, in turn, enhances the efficacy of the composition in killing organisms such as bacteria and viruses.

It may occur to one skilled in the art of polymer science that a variety of methods are available for accomplishing surface area modification. Preferably, surface area enhancement is accomplished by a modified spinning or casting method. For instance, electrostatic spinning is a modified spinning technique which results in fraying of the fiber as it exits the spinerette. Alternatively, a polymer solution can be wet- or dry-spun to create a roughened fiber surface by controlling the solvent type and the polymer solution temperature. This technology is well known and has been applied, for example, in the manufacture of asymmetric membranes having roughened pores for dialysis. The size of the roughened pores is primarily controlled

by the speed of precipitation which, in turn, is controlled by solvent interaction parameters, temperature, etc.

The surface area of the polymer composition is further enhanced by tethering chains of antimicrobial groups to the outer surface of the individual polymer fibers. Preferably, molecular chains of quaternary ammonium pendent groups are fabricated to have at least one end adapted for attachment to a fiber surface. For instance, surface grafting may be accomplished by creating surface free radicals as initiation sites from peroxide generation (ozone or microwave). Alternatively, surface attachment of an interpenetrating network may be achieved using a monomer which swells the substrate polymer. The incorporation of tethered antimicrobial chains has the further benefit of enhancing the functionality of the composition. In particular, the tethered antimicrobial chains extend into the particular biological solution to bind to harmful bacterial and viral organisms. In contrast to known dressing compositions in which a monolayer (or near monolayer) of bactericidal compound is directly attached to a fiber surface, the chain structures of the present invention, which function like arms extending outwardly from the fiber surface, more effectively bind the antimicrobial sites to harmful organisms. Preferably, tethering is accomplished by grafting the antimicrobial chains directly to the matrix surface, or by selective adsorption of a copolymer to the matrix surface.

Grafting techniques are well known in the art. For example, quaternary ammonium compound grafting using the monomer trimethylammonium ethyl methacrylate to graft polymerize to a modified polyethylene surface is described by Yahaioui (Master's Thesis, University of Florida, 1986). Yahioui describes a grafting technique in which a plasma discharge is used to create free radicals which initiate polymerization of appropriate monomers. Selective adsorption of appropriate block copolymers can also be used.

In contrast to known compositions in which an antimicrobial structure is achieved by covalently bonding silane groups to the surface of the base polymer, the present invention incorporates a chemical structure which is based on polymerization (i.e., surface grafting) of monomers containing all carbon-carbon, carbon-oxygen and carbon-nitrogen main bonds, such as the dialkly, diallyl, quaternary ammonium compounds. Consequently, the composition of

the present invention results in a structure which is less prone to reacting with acids and bases produced by bacterial growth. As previously mentioned, such reactions can degrade the attachment between the matrix and antimicrobial groups. In instances where the composition is applied to a wound dressing, such degradation could result in antimicrobial agents detaching from the polymer matrix and entering a wound site. In some cases, this can have the deleterious effect of retarding wound healing.

In an alternate embodiment of the present invention, anionic antibactericidal groups are immobilized on the surface of a superabsorbant dressing to improve the antibactericidal efficacy of the dressing. The positive charge associated with quaternary ammonium groups, for example, can be neutralized by negative ions, such as chloride ions present in physiological fluids such as urine and plasma. For applications where the degree of neutralization will significantly reduce the effectiveness of the antibactericidal agent, anionic surface groups can be substituted for quaternary ammonium groups. Examples of chemical compounds that can be used to produce immobilized anionic surface groups include Triton-100, Tween 20 and deoxycholate. For instance, Triton-100 contains a free hydroxyl group which can be derivatized into a good leaving group, such as tosyl or chloride, and subsequently reacted with a base-treated polymer, such as methyl cellulose, to yield a surface immobilized non-ionic surfactant

Dimethyldiallyl ammonium chloride is one example of a suitable monomer which may be used with the present invention. This monomer, commonly referred to as DMDAC or DADMAC, is used in the fabrication of commercial flocculating polymers. Modifications of trialkyl(p-vinylbenzyl) ammonium chloride or the p-trialkylaminoethyl styrene monomers are also suitable. One such example is trimethyl(p-vinyl benzyl) ammonium chloride; the methyl groups of this monomer can be replaced by other alkyl groups to impart desired properties. Alternatively, methacrylate-based monomers may be used; however, they may suffer from hydrolytic instability under acidic and basic conditions in a fashion similar to the silane-based treatments of the prior art. Consequently, methacrylate-based monomers are not preferred.

While the preferred embodiments of the invention have been illustrated and described, it will be clear that the invention is not so limited. Numerous modifications, changes,

variations, substitutions and equivalents will occur to those skilled in the art without departing from the spirit and scope of the present invention as described in the claims.

We claim:

1. A dressing for absorbing biological fluids, comprising:

a superabsorbent polymer matrix having an enhanced surface area; and

a plurality of antimicrobial compounds coupled by non-siloxane bonds to said polymer matrix.

2. A dressing as recited in claim 1, wherein said plurality of antimicrobial compounds comprise quaternary ammonium compounds.

3. A dressing as recited in claim 1, wherein said antimicrobial compounds comprise chain-like structures tethered at one end to said polymer matrix.

4. A dressing as recited in claim 1, wherein said plurality of antimicrobial compounds are non-ionic compounds.

5. A dressing as recited in claim 1, wherein said dressing comprises a sanitary pad.

6. A dressing as recited in claim 1, wherein said dressing comprises a tampon.

7. A dressing as recited in claim 1, wherein said dressing comprises a bandage.

8. A method for fabricating an intrinsically antimicrobial absorbent dressing, comprising the steps of:

forming a superabsorbent synthetic polymer matrix having an enhanced surface area; and

attaching a plurality of antimicrobial compounds to the enhanced surface area of said polymer matrix.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/29091

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61F 13/15
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According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/445, 447; 602/46, 56; 604/307, 358, 360

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EAST

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim
Y	US 5,035,892 A (BLANK et al.) 30 July 1991, Abstract, col 1, lines 10-17, and col. 13 lines 25-32.	1-8

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

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(54) Title: INTRINSICALLY BACTERICIDAL ABSORBENT DRESSING AND METHOD OF FABRICATION

(57) Abstract: A superabsorbent polymer dressing having antimicrobial properties for use in fabricating wound dressings, sanitary napkins, tampons and the like, includes a synthetic polymer matrix fabricated to have an enhanced surface area. Antimicrobial compounds are coupled to the surface of the polymer matrix by non-siloxane bonds.

Intrinsically Bactericidal Absorbent Dressing and Method of Fabrication

Field of the Invention

This invention relates generally to absorbent dressings, and more particularly highly-absorbent synthetic polymer dressings having antimicrobial agents attached thereto.

Background of the Invention

Bacterial growth in absorbent dressings for wounds, urinary incontinence diapers, and menstruation pads can lead to serious medical complications as well as social difficulties. For example, bacterial growth in urinary incontinence diapers or menstruation pads usually produces strong, unpleasant odors that are socially unacceptable and can cause persons to alter their lifestyle. Conventional absorbent pads for urinary incontinence and menstruation are not inherently bactericidal. Consequently, the only way to avoid growth of bacteria in the absorbent dressings is to change them at frequent intervals, even if the absorbent capacity of the pad has not been reached. In the area of wound dressings, bacterial contamination of acute wounds and infection of chronic skin wounds are major clinical problems that can result in significant morbidity and, in severe cases, mortality. Conventionally, wound dressings have been designed to absorb wound fluids and yet provide a moist environment for promoting wound healing. However, such moist environments create a nutrient rich reservoir for bacterial growth in the dressing. Bacteria growing in the dressing can be shed back into the wound, increasing the risk of wound infection, or response to toxins, and producing strong, foul odors.

In an effort to address these problems, antibiotics or chemical disinfectants are frequently applied topically to wounds prior to covering the wound with a dressing. Alternatively, topical agents are sometimes applied directly to the surface of the dressing. To control foul odors, some known dressings incorporate charcoal powder to absorb molecules generating the foul odor. For some applications, topical application of antibacterial agents is not desirable. For instance, bactericidal agents applied topically to wound dressings have a tendency to seep into the wound being treated. Furthermore, many antimicrobial drugs, such as iodine, are cytotoxic and will retard wound healing if used repetitively or at high concentrations.

A composition comprising a superabsorbent polymer having a monolayer (or near monolayer) of silane antimicrobial agent in a covalent bonding relationship with the base polymer is disclosed in U.S. Patent No. 5,045,322. The composition may be in the form of flakes, strips, powders, filaments, fibers or films, and may be applied to a substrate in the form of a coating. The aforementioned composition is less apt to enter a wound vis-a-vis conventional topical treatment systems. In that respect, the disclosed composition provides an improvement over conventional topical treatment systems. However, silanes contain siloxane bonds which can be cleaved by acids and bases produced by infection or bacterial growth. In turn, these reactions may weaken or destroy bonds between the silane antimicrobial agent and the underlying polymer. Consequently, antimicrobial agent may seep into a wound and retard wound healing.

The need exists for an improved antimicrobial dressing composition having an antimicrobial agent which can be maintained securely attached to a superabsorbent polymer upon exposure to acids and bases produced by infection and bacterial growth. In addition to reducing the propensity for detachment of the antimicrobial agent, it would be desirable to provide a surface area enhanced dressing structure for increasing the effectiveness of the antimicrobial agent.

Summary of the Invention

It is an object of the present invention to provide an inherently bactericidal superabsorbant dressing having an enhanced surface area.

It is another object of the present invention to provide an inherently bactericidal superabsorbant dressing having an improved bactericidal attachment structure that resists degradation upon exposure to acids or bases produced, for instance, during bacterial growth.

These and other objects are achieved by the inherently bactericidal polymer composition of the present invention. In the preferred embodiment, the composition comprises a polymer matrix having quaternary ammonium groups tethered to its surface through non-siloxane bonds. The surface area of the polymer matrix is enhanced, for instance, by electrostatically spinning a fiber-forming synthetic polymer to form a frayed fiber or filament. Alternatively, the polymer solution can be wet- or dry-spun to create a roughened fiber surface by controlling the choice of solvent and the polymer solution temperature. Additional surface area enhancement is provided by tethering molecular chains of quaternary ammonium pendent groups to the surface of the polymer matrix. Tethering may be accomplished by known techniques such as grafting and selective adsorption.

In an alternate embodiment of the invention, non-ionic bactericidal molecules are coupled to the surface of the polymer matrix, in lieu of ionically-charged molecules. Ionically-charged molecules are prone to being neutralized upon encountering oppositely-charged molecules. For instance, positively-charged quaternary ammonium groups may be neutralized by negatively-charged chloride ions present in physiological fluids. In instances were such neutralization is significant enough to reduce the bactericidal properties of the dressing below an acceptable level, non-ionic surface groups may be preferable.

Detailed Description of the Preferred Embodiments

A novel antibacterial, polymer composition is fabricated to have an enhanced surface area and superabsorbent capacity for biological fluids, including urine, blood, and wound exudate.

In the preferred embodiment of the present invention, the composition includes a polymer matrix having quaternary ammonium compounds attached to the surface of the polymer matrix. The polymer matrix is comprised of a plurality of hydrophilic fibers or filaments which can be fabricated in any suitable manner. For example, suitable fibers or filaments can be fabricated by wet- or dry-spinning a fiber-forming synthetic polymer from a spinning solvent. The resulting polymer has superabsorbent capacity. Generally, polymers capable of absorbing from about thirty to sixty grams of water per gram of polymer are considered to be superabsorbent. Examples of superabsorbent polymers which can be fabricated in this manner include polyacrylic acids, polyethylene oxides and polyvinyl alcohols. For example, methods for spinning polyethylene oxide using acetone solvent are well known.

Significantly, the polymer matrix is fabricated to have an enhanced surface area. Enhancing the surface area of the polymer matrix results in improved absorption of biological fluids, and increases the availability of sites for attachment of the antimicrobial quaternary ammonium compounds. A corresponding increase in the quantity and density of antimicrobial sites, in turn, enhances the efficacy of the composition in killing organisms such as bacteria and viruses.

It may occur to one skilled in the art of polymer science that a variety of methods are available for accomplishing surface area modification. Preferably, surface area enhancement is accomplished by a modified spinning or casting method. For instance, electrostatic spinning is a modified spinning technique which results in fraying of the fiber as it exits the spinerette. Alternatively, a polymer solution can be wet- or dry-spun to create a roughened fiber surface by controlling the solvent type and the polymer solution temperature. This technology is well known and has been applied, for example, in the manufacture of asymmetric membranes having roughened pores for dialysis. The size of the roughened pores is primarily controlled by the speed of precipitation which, in turn, is controlled by solvent interaction parameters, temperature, etc.

The surface area of the polymer composition is further enhanced by tethering chains of

antimicrobial groups to the outer surface of the individual polymer fibers. Preferably, molecular chains of quaternary ammonium pendent groups are fabricated to have at least one end adapted for attachment to a fiber surface. For instance, surface grafting may be accomplished by creating surface free radicals as initiation sites from peroxide generation (ozone or microwave). Alternatively, surface attachment of an interpenetrating network may be achieved using a monomer which swells the substrate polymer. The incorporation of tethered antimicrobial chains has the further benefit of enhancing the functionality of the composition. In particular, the tethered antimicrobial chains extend into the particular biological solution to bind to harmful bacterial and viral organisms. In contrast to known dressing compositions in which a monolayer (or near monolayer) of bactericidal compound is directly attached to a fiber surface, the chain structures of the present invention, which function like arms extending outwardly from the fiber surface, more effectively bind the antimicrobial sites to harmful organisms. Preferably, tethering is accomplished by grafting the antimicrobial chains directly to the matrix surface, or by selective adsorption of a copolymer to the matrix surface.

Grafting techniques are well known in the art. For example, quaternary-ammonium compound grafting using the monomer trimethylammonium ethyl methacrylate to graft polymerize to a modified polyethylene surface is described by Yahaioui (Master's Thesis, University of Florida, 1986). Yahioui describes a grafting technique in which a plasma discharge is used to create free radicals which initiate polymerization of appropriate monomers. Selective adsorption of appropriate block copolymers can also be used.

In contrast to known compositions in which an antimicrobial structure is achieved by covalently bonding silane groups to the surface of the base polymer, the present invention incorporates a chemical structure which is based on polymerization (i.e., surface grafting) of monomers containing all carbon-carbon, carbon-oxygen and carbon-nitrogen main bonds, such as the dialkly, diallyl, quaternary ammonium compounds. Consequently, the composition of the present invention results in a structure which is less prone to reacting with acids and bases produced by bacterial growth. As previously mentioned, such reactions can degrade the attachment between the matrix and antimicrobial groups. In instances where the composition is applied to a wound dressing, such degradation could result in antimicrobial agents detaching from the polymer matrix and entering

a wound site. In some cases, this can have the deleterious effect of retarding wound healing.

In an alternate embodiment of the present invention, anionic antibactericidal groups are immobilized on the surface of a superabsorbant dressing to improve the antibactericidal efficacy of the dressing. The positive charge associated with quaternary ammonium groups, for example, can be neutralized by negative ions, such as chloride ions present in physiological fluids such as urine and plasma. For applications where the degree of neutralization will significantly reduce the effectiveness of the antibactericidal agent, anionic surface groups can be substituted for quaternary ammonium groups. Examples of chemical compounds that can be used to produce immobilized anionic surface groups include Triton-100, Tween 20 and deoxycholate. For instance, Triton-100 contains a free hydroxyl group which can be derivatized into a good leaving group, such as tosyl or chloride, and subsequently reacted with a base-treated polymer, such as methyl cellulose, to yield a surface immobilized non-ionic surfactant.

Dimethyldiallyl ammonium chloride is one example of a suitable monomer which may be used with the present invention. This monomer, commonly referred to as DMDAC or DADMAC, is used in the fabrication of commercial flocculating polymers. Modifications of trialkyl (p-vinylbenzyl) ammonium chloride or the p-trialkylaminoethyl styrene monomers are also suitable. One such example is trimethyl (p-vinyl benzyl) ammonium chloride; the methyl groups of this monomer can be replaced by other alkyl groups to impart desired properties. Alternatively, methacrylate-based monomers may be used; however, they may suffer from hydrolytic instability under acidic and basic conditions in a fashion similar to the silane-based treatments of the prior art. Consequently, methacrylate-based monomers are not preferred.

While the preferred embodiments of the invention have been illustrated and described, it will be clear that the invention is not so limited. Numerous modifications, changes, variations, substitutions and equivalents will occur to those skilled in the art without departing from the spirit and scope of the present invention as described in the claims.

We claim:

1. A dressing for absorbing biological fluids, comprising:

a superabsorbent polymar matrix having an enhanced surface area; and

a plurality of antimicrobial compounds coupled by non-siloxane bonds to said polymer matrix.

2. A dressing as recited in claim 1, wherein said plurality of antimicrobial compounds comprise quaternary ammonium compounds.

3. A dressing as recited in claim 1, wherein said antimicrobial compounds comprise chain-like structures tethered at one end to said polymer matrix.

4. A dressing as recited in claim 1, wherein said plurality of antimicrobial compounds are non-ionic compounds.

5. A dressing as recited in claim 1, wherein said dressing comprises a sanitary pad.

6. A dressing as recited in claim 1, wherein said dressing comprises a tampon.

7. A dressing as recited in claim 1, wherein said dressing comprises a bandage.

8. A method for fabricating an intrinsically antimicrobial absorbent dressing, comprising the steps of:

forming a superabsorbent synthetic polymer matrix having an enhanced surface area; and

attaching a plurality of antimicrobial compounds to the enhanced surface area of said polymer matrix.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/29091

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61F 13/15
US CL :604/358

According to International Patent Classification (IPC) or to both national classification and IPC

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Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/445, 447; 602/46, 56; 604/307, 358, 360

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Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EAST

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Date of the actual completion of the international search	Date of mailing of the international search report
25 FEBRUARY 2000	04APR2000
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer A. T. NGUYEN Telephone No. (703) 308-2154

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